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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,047	04/14/2006	Katsuyuki Hamada	TSU-006	8849

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KIRK HAHN
14431 HOLT AVE
SANTA ANA, CA 92705

EXAMINER	
HILL, KEVIN KAI	

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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,047	HAMADA ET AL.	
	Examiner	Art Unit	
	Kevin K. Hill, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *7-9,13,14 and 17-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10-12,15,16 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. Applicant's response to the Requirement for Restriction, filed on August 20, 2007 is acknowledged.

Applicant has elected the following species without traverse, wherein:

i) the virus is adenovirus, as recited in claim 2;

ii) the carrier cell is A549, as recited in claims 4 and 21-23;

iii) the promoter is 1A1.3B, as recited in claim 5;

iv) the therapeutic compound is atelocollagen, as recited in claim 6 and 16;

v) the viral administration rate of the virus for immunological treatment is set between about 10^5 viral particles and 10^{11} viral particles for a patient with antibody negative to the virus, as recited in claim 12.

Because Applicant did not distinctly and specifically point out the supposed errors in the Group or species restriction requirement, the election has been treated as an election without traverse and the restriction and election requirement is deemed proper and therefore made final (MPEP § 818).

Claims 7-9, 13-14 and 17-19 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 1-6, 10-12, 15-16 and 20-23 are under consideration.

Priority

2. This application is a 371 of PCT/JP04/15220, filed October 15, 2003. A certified copy of PCT/JP04/15220, filed October 15, 2003, is filed with the instant application. Accordingly, the effective priority date of the instant application is granted as October 15, 2003.

Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) of JP 2003-354983, filed October 15, 2003. A certified copy of JP 2003-354983 has not been filed with the instant application.

Information Disclosure Statement

Applicant has filed an Information Disclosure Statement on March 26, 2007 that has been considered. The signed and initialed PTO Form 1449 is mailed with this action.

Specification

3. **The disclosure is objected to because of the following informalities:** the non-patent and patent literature citations (pg 2, [0007]; pg 17, [0036]) are incomplete. If printed publications are cited, the author (if any), title, date, pages or plates, and place of publication, or place where a copy can be found, will be given. See MPEP 707.05 (See, for example, pg 14, [0029]).

The specification appears to be a literal translation into English from a foreign document and is replete with grammatical and idiomatic errors. For example, the phrase "at the upper stream" should more correctly state "upstream" (pgs 28-29, joining ¶).

Appropriate correction is required.

Claim Objections

4. **Claims 1, 3-4, 10 and 20-23 are objected to because of the following informalities:**

With respect to claims 1 and 10, the claims identify CTL as a reaction that is to be induced in the claimed inventions. However, the claims do not first identify the reaction by its complete name prior to using its acronym. The abbreviation should be spelled out in the first appearance of the claims and should be followed by the abbreviation in parentheses, e.g. Epidermal Growth Factor (EGF).

With respect to claims 3-4 and 20-23, Applicant is advised that should claims 3 and 4 be found allowable, claims 20-23 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In the instant case, claim 20 recites the same limitation regarding the virus for immunological treatment as in claim 3, wherein both claims 3 and 20 are dependent on the virus for immunological treatment recited in claim 1.

Similarly, claims 21-23 recite the carrier cell type recited in claim 4, wherein claims 4 and 21-23 are dependent on the carrier cell recited in claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

5. **Claims 1, 10-11 and 15-16 are rejected under 35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

With respect to claim 1, the claim recites multiple administration steps, and thus it is unclear which cell is to be infected with the virus, and when the infection(s) is/are to occur. Is the virus for immunological treatment the same as or different from the oncolytic virus? Furthermore, what is the subject to the induced CTL response is directed in claims 1, 10 and 11? Is the claimed oncolytic virus a component of the drug composition or a separate agent? It is unclear what Applicant means by the recitation "to administration of a carrier cell".

The claim recites "a cancer gene therapeutic drug", indicating a single composition. However, the specification discloses that the claimed invention is actually "a drug kit for cancer therapy" (pg 3, [0010]; pg 4, [0015]) because the two agents, the "virus for immunological treatment" and the "carrier cell" are separate agents and administered separately.

As presently written, claim 1 recites a composition comprising two elements, a virus and a cell, wherein the recitation of intended use for the virus and the cell do not carry patentable weight because such features are considered inherent properties of the virus and the cell, absent evidence to the contrary.

With respect to claim 10, the claim recites the intended infection of the carrier cell with an oncolytic virus. However, as presently written, the method does not **require** the cell to be

infected with the oncolytic virus. The intended infection does not carry patentable weight regarding the structural limitations of the claimed cell in the composition.

With respect to claim 11, it is unclear what the reference date is, e.g. about two to not more than thirteen weeks from what date and/or method step?

With respect to claims 15-16, the claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. In particular, the claims recite the step of "administrating". However, the term 'administrating' is an executive or bureaucratic activity (www.thefreedictionary.com/administrating; last visited October 4, 2007). The Examiner respectfully suggests amending 'administrating' to 'administering'.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the Applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. **Claims 1-3, 20 are rejected under 35 U.S.C. 102(b)** as being anticipated by Kikuchi et al (Blood 100:3950-3959, 2002; available online July 25, 2002).

To the extent that the claim, as presently written, recites a composition comprising two structural elements, a virus and a cell, wherein the recitation of intended use for the virus and the cell do not carry patentable weight because such features are considered inherent properties of the virus and the cell, absent evidence to the contrary, the instant prior art rejection is applied.

Kikuchi et al teach a drug kit for cancer therapy, the kit comprising a replication-deficient adenovirus and dendritic cells (pg 3951, Methods; pg 3953, col. 2, Synergistic anti-tumor effects).

7. **Claims 1-3, 10-12, 15 and 20 are rejected under 35 U.S.C. 102(e)** as being anticipated by Terman, 2002/0177551 A1.

With respect to claims 1 and 10, Terman discloses a cancer therapeutic drug and a method of treating tumors such as carcinoma, melanoma, sarcoma, leukemia and lymphoma (pg 8, [0055]), the method comprising a step of administering to a patient *in vivo* with a nucleic acid viral vector to induce a CTL reaction to a carrier cell expressing one or more desired antigens, e.g. a tumor antigen, and after a predetermined period of time, the method further comprising a step of administering to said patient carrier cells infected with an oncolytic virus (pg 54, [0544, 0549]; pg 90-91, [1057-1058, 1060, Example V]), wherein said carrier cell may be a tumor cell (pg 8, [0052]).

With respect to claim 2, Terman discloses the virus may be an adenovirus (pg 10, [0075]; pg 11, [0082], [0086]).

With respect to claims 3 and 20, Terman discloses the virus may be replication-selective or inactivated (pg 54, [0556]; pg 161, [2087]).

With respect to claim 11, Terman discloses the predetermined period of time to be, for example, at least three weeks (pg 94, Table V).

With respect to claim 12, Terman discloses the use of 10^{10} virus particles (pg 159, [2067]).

With respect to claim 15, Terman discloses the carrier cell to be administered to the patient into the host tumor (pg 90, [1056]).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. **Claims 1-4, 10-12, 15 and 20-23 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Terman (2002/0177551 A1) and Harrison et al (Human Gene Therapy 12(10): 1323-1332, 2001).

Terman discloses a cancer therapeutic drug and a method of treating tumors such as carcinoma, melanoma, sarcoma, leukemia and lymphoma (pg 8, [0055]), the method comprising a step of administering to a patient *in vivo* with 10^{10} virus particles (pg 159, [2067]) comprising a nucleic acid viral vector to induce a CTL reaction to a carrier cell expressing one or more desired antigens, e.g. a tumor antigen, and after a predetermined period of time, e.g., at least three weeks (pg 94, Table V), the method further comprising a step of administering to said patient carrier cells infected with an oncolytic virus (pg 54, [0544, 0549]; pg 90-91, [1057-1058, 1060, Example V]), wherein said carrier cell may be a tumor cell (pg 8, [0052]), wherein the carrier cell is administered to the patient into the host tumor (pg 90, [1056]). Terman discloses the nucleic acid viral vector and oncolytic virus may be an adenovirus (pg 10, [0075]; pg 11, [0082], [0086]) and may be replication-selective or inactivated (pg 54, [0556]; pg 161, [2087]).

Terman does not disclose the carrier cell to be an A549 cell. However, at the time of the invention, Harrison et al taught the use of A549 cells to produce oncolytic adenoviruses in a method to treat tumors. Absent evidence to the contrary, nothing non-obvious is seen with

substituting one tumor cell for another tumor cell because the simple substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each tumor cell would be capable of allowing replication and production of replication-selective oncolytic viruses, for example.

Thus, the invention as a whole is *prima facie* obvious.

9. **Claims 1, 6, 10 and 16 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Terman (2002/0177551 A1) and Harrison et al (Human Gene Therapy 12(10): 1323-1332, 2001), claims 1-4, 10-12, 15 and 20-23 above, and in further view of Ochiya et al (Curr. Gene Therapy 1: 31-52, 2001).

The prior cited art does not teach the kit or method to comprise atelocollagen. However, at the time of the invention, Ochiya et al reviewed the advantages of using atelocollagen to mediate controlled-release of bioactive agents of molecular medicines (pg 33, Figure 1). Ochiya et al teach that atelocollagen may be designed to degrade in vivo or be surgically removed (pg 38, Figure 5), is useful for the prolonged release of adenovirus vectors in vivo (pgs 40-41), and may be used as a carrier for cell-based therapies (pgs 46-47, Figure 12).

It would have been obvious to one of ordinary skill in the art to combine atelocollagen with the virus and cell as taught Terman with a reasonable chance of success because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Thus, the invention as a whole is *prima facie* obvious.

10. **Claims 1 and 5 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Terman (2002/0177551 A1), Harrison et al (Human Gene Therapy 12(10): 1323-1332, 2001) and Ochiya et al (Curr. Gene Therapy 1: 31-52, 2001), as applied to claims 1-4, 6, 10-12, 15-16 and 20-23 above, and in further view of Alemany et al (U.S. Patent 6,403,370 B1) and Barker et al (Genomics 38:215-222, 1996).

The prior cited art does not teach the oncolytic virus to comprise a 1A1.3B promoter. However, at the time of the invention, Alemany et al disclosed a method for killing tumor target cells, the method comprising an oncolytic adenoviral vector, wherein the oncolytic adenoviral vector comprises a tumor cell-activated promoter operably linked to the adenoviral E1 gene (col. 6, lines 24-37).

Alemany et al do not disclose the use of a 1A1.3B promoter. However, at the time of the invention, Barker et al taught that the identification of the promoter region for 1A1.3B and that 1A1.3B (also known as CA125) is an art-recognized ovarian cancer marker antigen.

It would have been obvious to one of ordinary skill in the art to substitute a tumor cell-activated promoter as taught by Terman for a 1A1.3B promoter as taught by Barker et al with a reasonable chance of success because the art recognized that products of the adenovirus E1 gene control the replication of the adenovirus vector in tumor cells, and thus the use of a tumor cell-activated promoter to regulate the expression of E1 gene products would confer or enhance specificity of viral replication in the tumor cells. The art also recognized the existence of many tumor-activated promoters, including 1A1.3B, wherein the 1A1.3B gene product is an art-recognized ovarian cancer marker antigen. Absent evidence to the contrary, nothing non-obvious is seen with substituting one tumor cell-activated promoter for another tumor cell-activated promoter because the simple substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each tumor cell-activated promoter would be capable of regulating the expression of E1 gene products so as to confer or enhance specificity of viral replication in the tumor cells..

Thus, the invention as a whole is *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined

application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. **Claims 1-6 and 20-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting** as being unpatentable over claims 1-5 of copending Application No. 10/575,894. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed cancer gene therapeutic drug in the co-pending application comprises the same structural elements as recited in the instant application, specifically an oncolytic adenovirus comprising a 1A1.3B promoter, an A549 carrier cell and atelocollagen.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kevin K. Hill

Q. JANICE LI, M.D.
PRIMARY EXAMINER